Cryo electron microscopy

Capability, Limitation and Potential Solutions

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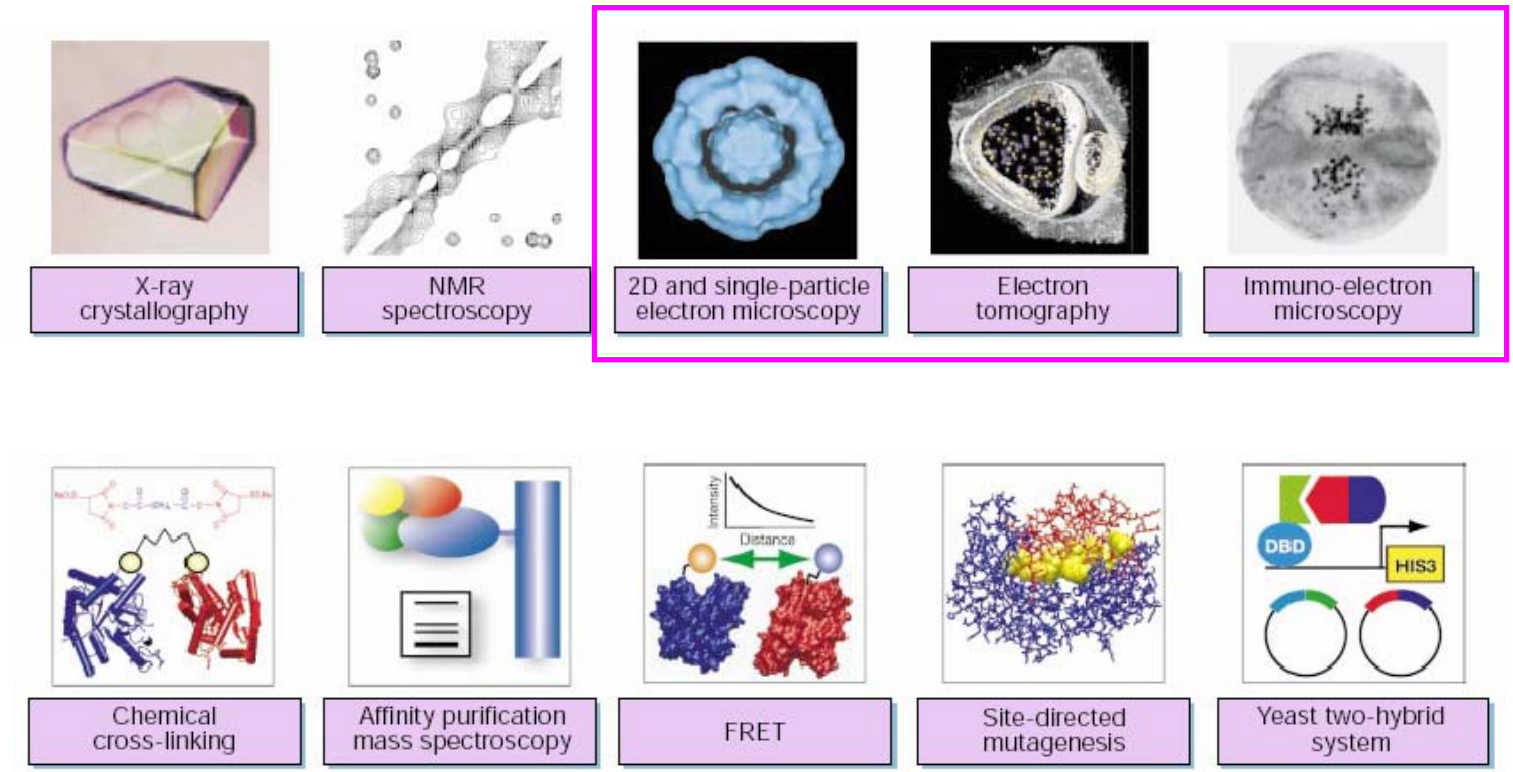
Cryo-EM - where does it stand in molecular biology?



Sali, et al. Nature, 2003

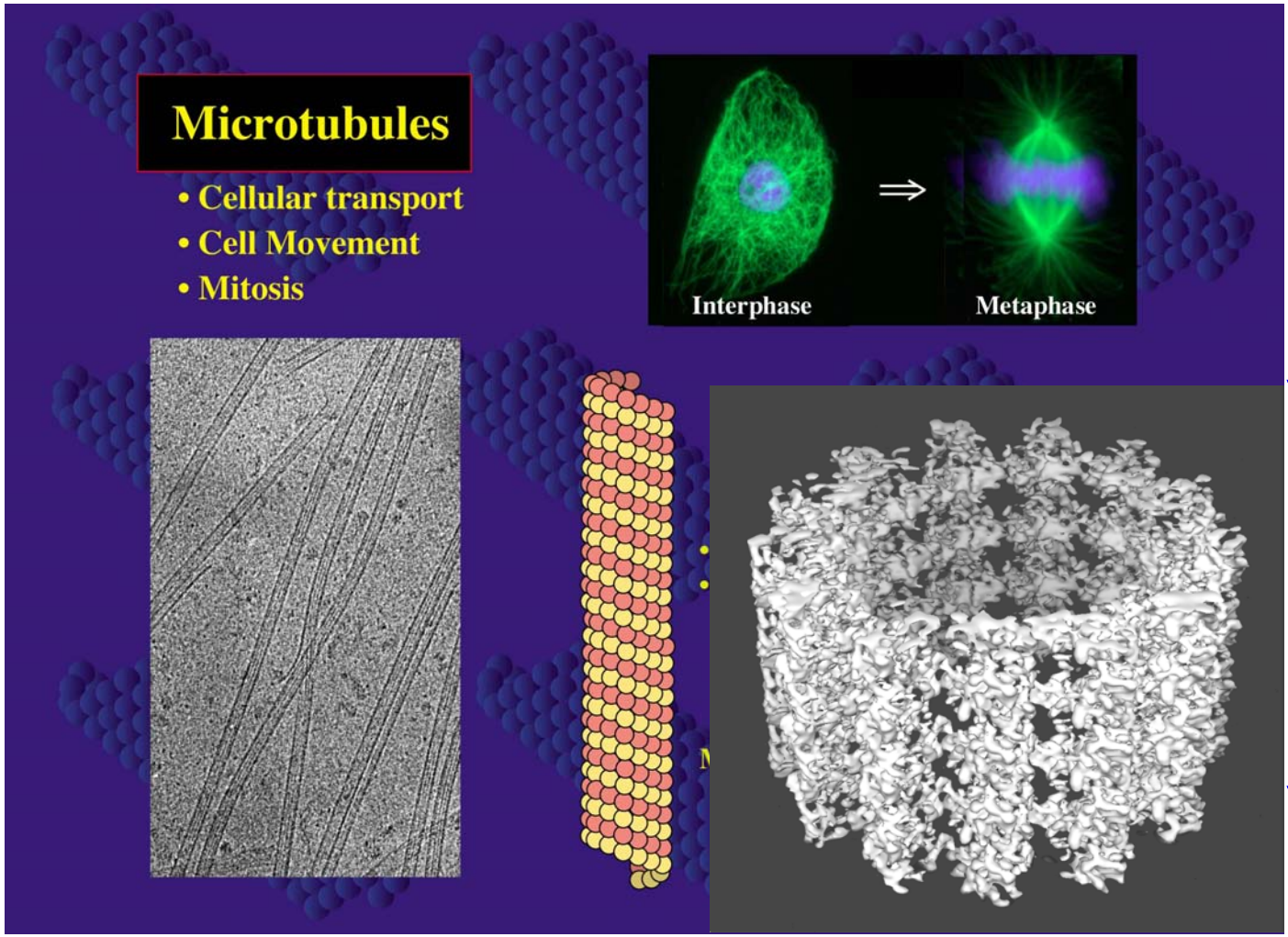
Cryo-EM

Samples: purified molecular complexes and microbes

Resolution: 0.35 - 8nm

Biomedical application: structure - function correlation

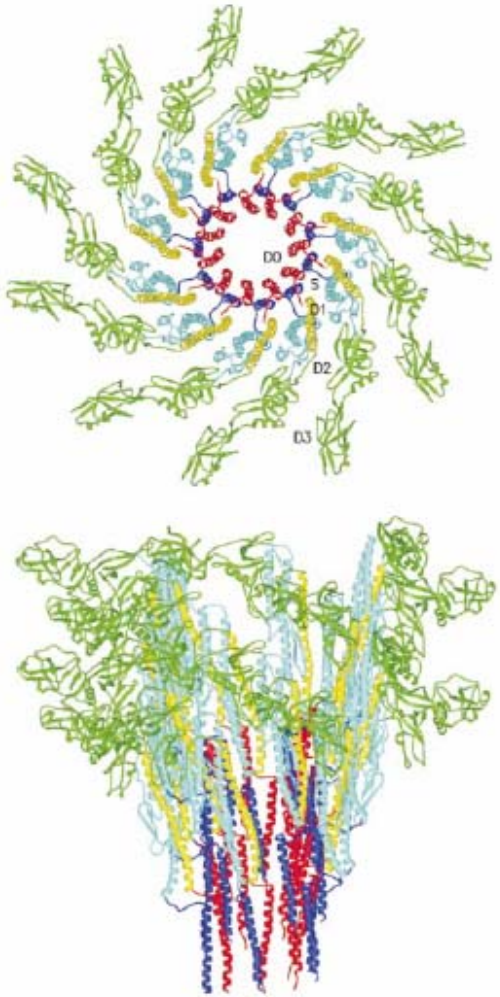
Sample prep: vitrification



Li, et al. Structure, 2002

Atomic Models of ACh-Receptor and Flagellum by Cryo-EM

Miyazawa, et al. Nature, 2003



Yonekura, et al. Nature, 2003

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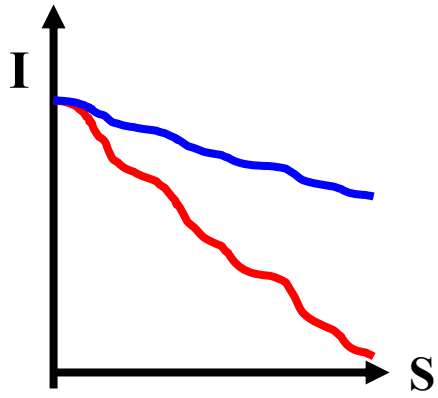
Cryo-EM - current limitations

Biggest Problem - 80-90% signal loss

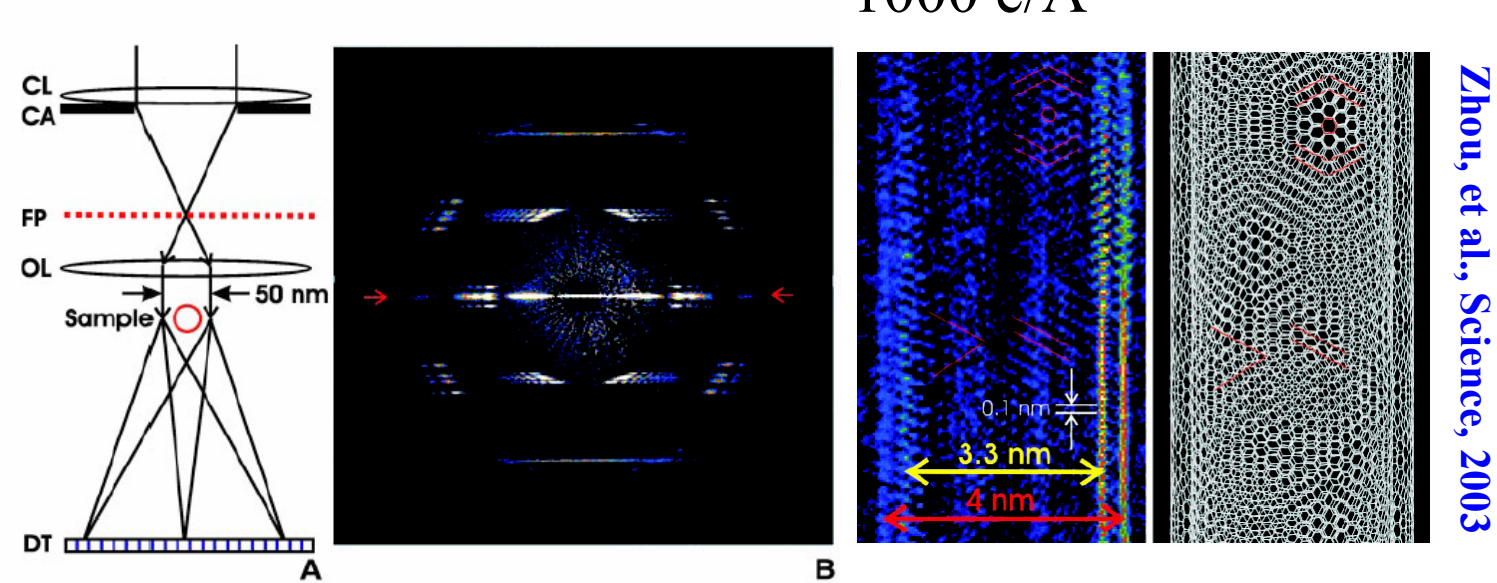
(a) specimen movement and charging
(b) modulation transfer function of the film and densitometer
(c) partial coherence of the electron source
(d) depth of focus
(e) beam tilt (f) particle image alignment error



Potential solutions

(1) EM automation and supercomputing
(2) Diffraction imaging

1000 e/Å^2



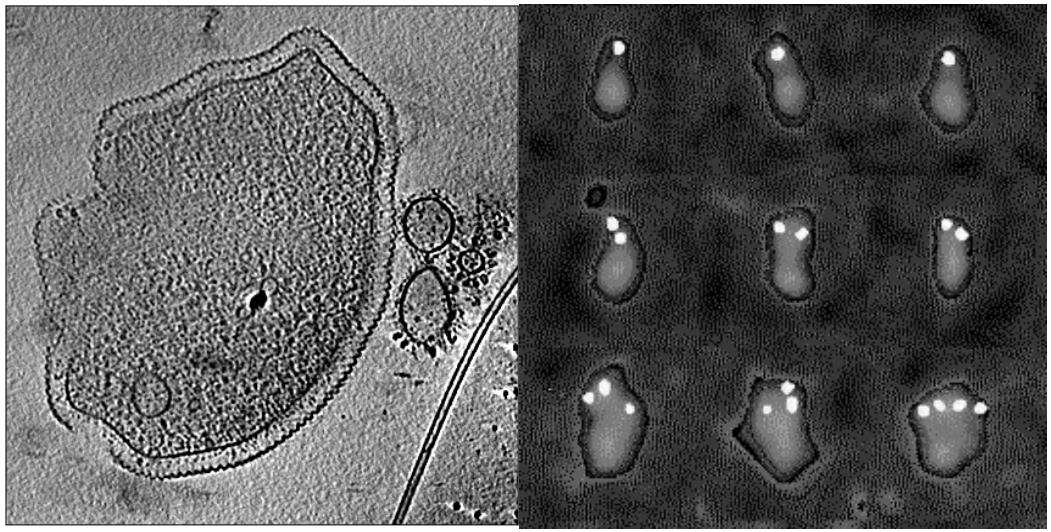
Zhou, et al., Science, 2003

Cryo-EM - Protein Localization in Microbial Cells

Practical problem in imaging microbial cells by tomography

molecular crowding

QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.



Potential solution: electron dense labeling

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